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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,432	02/14/2006	Andrew Cassidy	056291-5231	2301

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
BAUGHMAN, MOLLY E	
ART UNIT	**PAPER NUMBER**
1637	
MAIL DATE	**DELIVERY MODE**
12/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,432	CASSIDY ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87* is/are pending in the application.

4a) Of the above claim(s) *1-55 and 67-87* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/14/06; 7/31/06; 6/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 56-66, in the reply filed on 10/5/2007 is acknowledged.

2. Claims 1-55, and 67-87 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/5/2007.

3. Claims 56-66 are currently under examination.

Priority

4. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119 (a-d), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35

U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its

inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 2/14/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

a. Citation, Hu et al., has fully been considered, however, it has been lined through to avoid duplicate reference listings at time of print.

6. The information disclosure statement (IDS) submitted on 7/31/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

b. Citation Nos. 2-3, 27, 29, 34, 47-48, and 56 have fully been considered, however, have been lined through to avoid duplicate reference listings at time of print.

7. The information disclosure statement (IDS) submitted on 6/28/2007 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, some citations have been either modified, or lined through for the following reasons:

c. All of the citations have fully been considered, however, they all have been lined through to avoid duplicate reference listings at time of print.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 56-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim(s) 56-66 is/are confusing because it cannot be determined what is encompassed by, "a first strand cDNA synthesis hybridized to RNA." The phrase describing the cDNA part of the cDNA-RNA hybrid is grammatically unclear as it appears to be functional language of a reaction versus an actual product. Clarification is required. While claims 57-59, and 63-64 do not particularly use the phrase, they depend from claims which use the phrase.

b. Claim 64 is confusing because it is unclear how the cDNA-mRNA hybrid further comprises an amplification primer. The cDNA-mRNA hybrid comprises a

cDNA strand, RNA strand, and template switching oligonucleotide, hybridized together in various orientations, however, it is unclear how the amplification primer is associated with the hybrid.

Claim 65 is confusing because it is unclear how the claim is further limiting. The claim is drawn to language describing a method, (i.e." the 3' end of the first strand cDNA synthesis is extended such that it is substantially complementary to the template switching oligonucleotide") and therefore, it is unclear how the claim further limits the actual product, a cDNA-mRNA hybrid.

Claim Interpretation

Initially, it is noted that MPEP 2111 states that, "During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. In re Morris, 12'7 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997); In re Prater, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969)." As such, for the purposes of examination, it is submitted that "wherein the first strand cDNA synthesis is synthesized by a reverse transcriptase...," in claim 66, will be interpreted and examined based only on the product (a cDNA-mRNA hybrid) and not how the product was formed (i.e. via a reverse transcriptase). The patentability of the product relies on the physical and functional characteristics of the product itself and not how it was formed. See In re Brown 459 F.2d 531,535, 173 USPQ 685, 688 (CCPA 1972):

"As a practical matter the Patent Office is not equipped to manufacture products by the myriad

of processes put before it and then obtain prior art products and make physical comparisons therewith....Once the examiner provides a rationale to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with EVIDENCE establishing an unobvious difference between the claimed product and the prior art product."

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 56-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhu et al. (US 6,465,219) in view of Chenchik et al., (1998), "Generation and Use of High-Quality cDNA from Small Amounts of Total RNA by SMART PCR," Natick, MA: BioTechniques Books (of record), ***or*** Petalidis et al., "Global amplification of mRNA by

template-switching PCR: linearity and application to microarray analysis," Nucleic Acids Research, Nov. 2003, Vol.31, No.22, e142, pp.1-7, ***or*** Chenchik et al. (US 5,962,272).

Regarding claim 56 and 66, Zhu et al. teach a cDNA-RNA hybrid comprising a first strand cDNA synthesis hybridized to RNA wherein the cDNA comprises from the 5'end, an RNA polymerase promoter operably linked to an RNA annealing region, and wherein at least one non-templated nucleotide at the 3' end of the first strand cDNA is hybridized to a template switching oligonucleotide (i.e. "TSO") (see col.1, lines 57-64, where the antisense primer complex comprises 5' to 3', an RNA promoter sequence operably linked to an antisense primer sequence (i.e. an RNA annealing region), and a universal priming site; col.2, lines 66-67 - col.3, lines 1-11; and col.11, lines 37-52, where the universal priming site is added to the 3' end of the antisense cDNA strands, which are hybridized to the mRNA molecules, via a TSO (inherently requiring at least one non-templated nucleotide on the cDNA strand for hybridization).

Zhu et al. do not teach the cDNA-RNA hybrid comprising an amplifier sequence 5' to the RNA polymerase promoter, and wherein the amplifier sequence and the TSO contain the same sequence.

Chenchik et al. (1998, Biotechniques Books), referred to herein as "Chenchik 1," teach a cDNA-RNA hybrid comprising a first strand cDNA synthesis hybridized to RNA wherein the cDNA comprises from the 5'end, an amplifier sequence, an RNA annealing region, and wherein at least one non-templated nucleotide at the 3' end of the first strand cDNA is hybridized to a TSO, and wherein the amplifier sequence and the TSO contain the same sequence (see "cDNA synthesis primer" and the "TS oligonucleotide"

in the Materials and Reagents on pg.306, wherein both the amplifier and the TSO contain the same sequence, and Figure 3, the cDNA-RNA hybrid before "Template switching and extension by RT,").

Petalidis et al. teach a cDNA-RNA hybrid comprising a first strand cDNA synthesis hybridized to RNA wherein the cDNA comprises from the 5'end, an amplifier sequence, an RNA annealing region, and wherein at least one non-templated nucleotide at the 3' end of the first strand cDNA is hybridized to a TSO, and wherein the amplifier sequence and the TSO contain the same sequence (see pg.2, "Preparation of amplified labeled cDNA targets," where the cDNA synthesis strand comprises "SMART CDS primer IIA" and the template switching primer, wherein both the amplifier and TSO contain the same sequence).

Chenchik et al. (US 5,962,272), referred to herein as "Chenchik 2," teach a cDNA-RNA hybrid comprising a first strand cDNA synthesis hybridized to RNA wherein the cDNA comprises from the 5'end, an amplifier sequence, an RNA annealing region, and wherein at least one non-templated nucleotide at the 3' end of the first strand cDNA is hybridized to a TSO, and wherein the amplifier sequence and the TSO contain the same sequence (see Example 4, col. 19-20, particularly Step 1, the cDNA synthesis strand of the cDNA-RNA hybrid comprises the "cDNA synthesis primer (oligo d(T) primer CDS3," and the TSO comprises the "CAPswtich oligonucleotide (Na1smG3)," wherein both the amplifier and TSO contain the same sequence).

Regarding claim 57, Zhu et al. teach the cDNA-RNA hybrid, wherein the RNA polymerase promoter is a bacteriophage promoter selected from the group consisting of T7, T3 and SP6 (see col.3, lines 8-11; and col.10, lines 11-33).

Regarding claim 58, Zhu et al. teach the cDNA-RNA hybrid, wherein the RNA annealing region comprises poly (dT) of about 10 to about 30 T residues in length (see col.10, lines 53-60).

Regarding claim 59, Chenchik 1, Petalidis, and Chenchik 2 all teach the cDNA-RNA hybrid, wherein the 3' end of the RNA annealing region comprises a VN clamp, wherein V is A, G or C and N is A, G,C or T (see Chenchik 1, pg.306, "Materials and Reagents;" Petalidis, pg.2, "Preparation of amplified labeled cDNA targets;" and Chenchik 2, col.18, lines 19-24).

Regarding claim 60, Chenchik 1, Petalidis, and Chenchik 2 all teach the cDNA-RNA hybrid, wherein at least one non-templated nucleotide at the 3' end of the first strand cDNA synthesis is deoxycytidine (see Chenchik 1, pg.314, Figure 3; Petalidis, pg.2, "Preparation of amplified labeled cDNA targets," wherein the TSO comprises a '3 -GGG- sequence which inherently must hybridize to deoxycytidine(s) on the cDNA strand; and Chenchik 2, col.18, lines 19-24, and col.20, lines 19-40, wherein the TSO comprises a '3 -GGG- sequence which inherently must hybridize to deoxycytidine(s) on the cDNA strand).

Regarding claims 61 and 62, Chenchik 1, Petalidis, and Chenchik 2 all teach the cDNA-RNA hybrid, wherein at least three non-templated nucleotide at the 3' end of the first strand cDNA synthesis are hybridised to a template switching oligonucleotide, and

wherein at least three of the non-templated nucleotides at the 3' end of the first strand cDNA synthesis are deoxycytidine nucleotides (see Chenchik 1, pg.314, Figure 3; Petalidis, pg.2, "Preparation of amplified labeled cDNA targets," wherein the TSO comprises a '3 -GGG- sequence which inherently must hybridize to deoxycytidine(s) on the cDNA strand; and Chenchik 2, col.18, lines 19-24, and col.20, lines 19-40, wherein the TSO comprises a '3 -GGG- sequence which inherently must hybridize to deoxycytidine(s) on the cDNA strand).

Regarding claim 63, Chenchik 1, Petalidis, and Chenchik 2 all teach the cDNA-RNA hybrid, wherein the template switching oligonucleotide has at least three guanine residues at its 3' end (see Chenchik 1, pg.314, Figure 3; Petalidis, pg.2, "Preparation of amplified labeled cDNA targets," wherein the TSO comprises a '3 -GGG- sequence; and Chenchik 2, col.18, lines 19-24, and col.20, lines 19-40, wherein the TSO comprises a '3 -GGG- sequence).

Regarding claim 64, Chenchik 1, Petalidis, and Chenchik 2 all teach the cDNA-RNA hybrid, further comprising an amplification primer and wherein, the amplification primer contains the same sequence as the amplifier sequence and the template switching oligonucleotide (see Chenchik 1, pg.306, "Materials and Reagents," the PCR primer; Petalidis, pg. 2, "Preparation of amplified labeled cDNA targets," the PCR primer; and Chenchik 2, col.20, lines 50-52, the PCR primer (Na1sm)).

One of ordinary skill in the art would have been motivated to modify the cDNA-RNA hybrid of Zhu et al. to further incorporate an amplifier sequence 5' to the RNA polymerase promoter sequence because Zhu et al. demonstrates the need for

incorporating sequences into the cDNA-RNA hybrid that can be used for later amplification, as he notes that the universal primer site (i.e. complementary sequence to the TSO) and the antisense primer complex sequence can serve "as anchors for efficient and sufficiently specific PCR amplification" (col.13, lines 19-25). Chenchik 1, Petalidis, and Chenchik 2 all demonstrate that it was conventional in the art at the time of the invention to incorporate amplifier sequences 5' to the RNA annealing region of the cDNA strand, which contain the same sequence as the TSO sequence and can be used in supplemental amplification using a single primer. Furthermore, Chenchik 1 states that attaching an arbitrary sequence to the 5' end of the cDNA by priming in order to create universal primer binding sites is more efficient and less complex than other methods, including adaptor ligation or homopolymer tailing, and allows such sequences to be incorporated in a single step, in a single tube and within an hour (see pg.306, second and third paragraphs; pg.313, second paragraph; pg.318, "Advantages and Limitations of the SMART Technology," first paragraph). Since Zhu et al. demonstrates the benefits of incorporating sequences into the cDNA-RNA hybrid that can be used for later amplification and Chenchik 1, Petalidis, and Chenchik 2 all demonstrate that it was conventional in the art at the time of the invention to incorporate amplifier sequences 5' to the RNA annealing region of the cDNA strand, which contain the same sequence as the TSO sequence and can be used in supplemental amplification using a single primer, it would have been obvious to one skilled in the art to add an amplifier sequence, containing the same sequence as the TSO sequence, 5' to the RNA polymerase promoter sequence to achieve the predictable result of incorporating sequences into the

cDNA-RNA hybrid that can be used for later amplification. Therefore, the skilled artisan would have had a reasonable expectation of success in incorporate an amplifier sequence 5' to the RNA polymerase promoter sequence in the cDNA-RNA hybrid of Zhu et al.. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed cDNA-RNA hybrid and include the claimed RNA amplifier sequence therein.

Summary

13. No claims are free of the prior art.

14. Rajeevan et al., "Global amplification of sense RNA: a novel method to replicate and archive mRNA for gene expression analysis," Genomics, Oct. 2003, Vol.82, No.4, pp.491-497 is noted as a reference of interest.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 12/13/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

12/13/07